



June 13, 2022

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Comments for Docket No. FDA-2021-D-0789, “Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials; Draft Guidance for Industry”

Dear Sir or Madam:

The American Society of Gene & Cell Therapy (ASGCT) appreciates the opportunity to comment on this important guidance document. ASGCT is a nonprofit professional membership organization comprised of more than 5,500 scientists, physicians, clinicians, and other professionals working in gene and cell therapy in settings such as universities, hospitals, and biotechnology companies.

The mission of ASGCT is to advance knowledge, awareness, and education leading to the discovery and clinical application of genetic and cellular therapies to alleviate human disease. Many of our members have spent their careers in this field performing the underlying research that has led to today’s robust pipeline of transformative therapies. By bringing together members from diverse backgrounds, ASGCT strives to be a catalyst for transformative medicine using genetic and cellular therapies to control and cure human disease. We appreciate FDA’s ongoing willingness to hear from stakeholders about ways to improve and adapt policies to consider the unique attributes of these therapies.

I. General Comments

ASGCT supports the Food and Drug Administration’s (FDA or the Agency) efforts to improve enrollment of historically underrepresented populations in clinical research and recognizes the issuance of this draft guidance as an important contribution towards this effort. ASGCT believes that more representative clinical trial populations are essential to properly understanding and evaluating the benefit-risk profile of innovative medical products, specifically cell and gene therapy products. Cell and gene therapy products are often developed to treat rare diseases, many of which have small patient populations and disproportionately affect minority populations. The guidance and actions by the Agency to expand diversity will need to account for the patient access issues related to rare diseases and ensure adequate flexibility in approaches.

ASGCT highlights the timing of the issuance of this draft guidance and notes that its issuance parallels similar legislative efforts in Congress. ASGCT recommends FDA consider current proposed legislation when preparing revised, final, or additional guidance on diversity to ensure it is aligned with any new statutory provisions.

In addition to the above comments, ASGCT provides these specific comments for the Agency's consideration.

II. Specific Comments

1. *Establishing Goals for Diversity and Representation in Small Patient Populations*

In considering the generally smaller trial populations for cell and gene therapy products, ASGCT requests the guidance address how representation should be defined in this context and how sponsors should develop diversity goals for these populations. ASGCT notes that the FDA recommends that diversity goals be based upon the epidemiology of the disease (lines 201-207). However, ASGCT believes that the concept of "epidemiology" is not well defined. ASGCT suggests the Agency acknowledge that diversity goals may be updated as new information and data is generated from a study of a particular drug in a population representative of the disease epidemiology.

ASGCT appreciates the Agency's recommendation that disease prevalence may also be used to establish enrollment goals (lines 213-214). However, ASGCT notes that prevalence for many rare diseases may not be well understood or available due to limited newborn screenings for many new disorders. Thus, ASGCT requests the Agency take a flexible and collaborative approach when assessing sponsors' enrollment goals.

In light of the current enrollment challenges in trials for cell and gene therapies for rare diseases, ASGCT believes there will likely be several cases where there is not enough clinical trial data to characterize the safety and efficacy of an investigational product, let alone differences in safety and efficacy for a specific racial or ethnic population. For these cases, ASGCT requests FDA clarify whether sponsors can use data from foreign countries to both evaluate the drug and identify any differential effects among racial or ethnic subgroups.

In addition, ASGCT recommends, for products with smaller patient populations, pre-market diversity plans should take into account potential post-market studies that can provide more diverse data and a better analysis. This would allow for more timely access to necessary treatments for patients while also providing a better understanding the effects on different subgroups. In addition to providing sponsors with another opportunity to assess a drug in a specific subgroup who may not have been well-represented in pre-market studies, the use of post-market studies to achieve enrollment

targets would likely not slow development or marketing approval of a product, which is particularly important for drugs for serious or life-threatening conditions with high unmet need.

2. *Content of Diversity Plan*

In addition to the sample list of trial enrollment and retention strategies provided in the guidance (Table 1, Category 4.B.), ASGCT requests the Agency recommend particular trial enrollment and retention strategies for sponsor's consideration. ASGCT recommends the Agency endorse strategies designed to build trust and generate interest in clinical research as well as increase access to clinical trial sites for historically underrepresented racial and ethnic populations. Recommended tactics include locating clinical trial sites in areas with greater concentrations of racial and ethnic minorities, encouraging the development and training of clinicians and principal investigators of diverse backgrounds, and supporting community outreach and educational initiatives.

3. *Criteria and Method for Reviewing Diversity Plans*

ASGCT notes that the Agency suggests sponsors seek feedback on their Diversity Plans "as soon as practicable," (lines 51-52) but does not recommend a specific mechanism or time for sponsors to interact with the Agency to seek feedback or provide updates on the Diversity Plan. Should the Agency include additional details on the suggested timing of the regulatory interaction in the finalized guidance, ASGCT recommends the Agency emphasize that the meetings occur before protocols and enrollment criteria are finalized.

In addition, ASGCT also seeks clarity on the criteria by which Diversity Plans will be evaluated. Specifically, ASGCT seeks to understand who at the FDA will be evaluating the Diversity Plans and whether the Office of Minority Health and Health Equity will be involved in the reviews. ASGCT also recommends that Diversity Plans be reviewed by both a clinical reviewer and an expert in diversity and inclusion in clinical research. It will also be imperative that the review of the Diversity Plans by FDA occur in a timely manner to ensure there is not a delay in the development of these critical medications.

Considering the enrollment challenges for trials for cell and gene therapy products, ASGCT urges the Agency to carefully consider the activities and strategies sponsors implement to increase enrollment when assessing a Diversity Plan.

4. *Barriers to Broader Enrollment*

ASGCT appreciates FDA's reference to the significant practical barriers that prevent participation of historically underrepresented racial and ethnic populations in clinical trials (lines 93-94). ASGCT supports efforts to offset the patients' financial costs of

participation as an effective solution to barriers to enrollment. The financial burden of travel, lodging, and lost wages can be a significant impediment to enrollment of patients, particularly for rare diseases and underrepresented populations.

ASGCT recommends that in addition to the above-mentioned costs that the financial burdens of childcare be added to the list of practical barriers to clinical trial participation. Specifically identifying childcare as a financial and logistical barrier to broader participation in clinical trials will make it easier for sponsors to ensure that reimbursement for childcare expenses will receive Institutional Review Board (IRB) approval.

Additionally, ASGCT recommends that FDA acknowledge the cultural and systemic barriers that have impeded enrollment of certain racial and ethnic populations in clinical research. Historic injustices and abuses of racial and ethnic minority populations by the clinical research enterprise has contributed to a general lack of trust in the healthcare system amongst these populations, which has undermined efforts to broaden enrollment. Towards this end, ASGCT emphasizes the importance of acknowledging these past injustices and working with principal investigators and clinical trial managers on communication and educational initiatives to build trust and increase enrollment. ASGCT believes that continual collaboration with principal investigators and clinical trial managers from diverse backgrounds is essential to developing trust.

5. Definitions of Race and Ethnicity

The Society recognizes that the FDA follows the Office of Management and Budget's (OMB) definitions for race and ethnicity. However, ASGCT notes that for the purposes of this guidance and for medical product development more generally, OMB's definitions and classifications are not broad enough and may not be reflective of the United States' population, especially considering that they have not been revised since 1997. More specifically, OMB's definitions do not include categories for multi-racial or multi-ethnic identities. Similarly, ASGCT also notes that the binary ethnic categorization of Hispanic or Not Hispanic can be confusing for clinical trial subjects, particularly those who identify as multi-ethnic. The guidance and Diversity Plan criteria will need to be adaptable and dynamic to accommodate the existing demographics and the changing populations in the future.

ASGCT recommends that the Agency consider developing a broader racial and ethnic classification scheme that includes multi-racial and multi-ethnic identities. This broader classification scheme will also assist in standardization and mapping race and ethnicity data to pre-existing datasets.



Thank you for the consideration of these comments. If you have any questions, please do not hesitate to contact Margarita Valdez Martínez, Director of Policy and Advocacy, at mvaldez@asgct.org.

Sincerely,

A handwritten signature in black ink, appearing to read 'David Barrett', is written over a horizontal line.

David Barrett, J.D.
Chief Executive Officer